Haemophilus influenzae meningitis

Jeffrey A Rumbaugh MD ( Dr. Rumbaugh of the Johns Hopkins University has no relevant financial relationships to disclose. )
Karen L Roos MD FAAN, editor. ( Dr. Roos of Indiana University School of Medicine has no relevant financial relationships to disclose.)

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Introduction

This article includes discussion of Haemophilus influenzae meningitis, Haemophilus influenzae, Haemophilus influenzae type b, Hib, H influenzae, and H flu. The foregoing terms may include synonyms, similar disorders, variations in usage, and abbreviations.

Overview

Meningitis is the most serious form of Haemophilus influenzae infection, historically causing significant mortality and morbidity, especially among children. Vaccination against H influenzae type b has dramatically decreased the impact of this disease, making recognition more difficult when it occurs. In this article, the author reviews the clinical manifestations and pathophysiology of H influenzae infection, with emphasis on the key features useful for making a timely diagnosis. Recent research has elucidated the factors involved in the inflammatory response to this organism, and new PCR-based techniques for confirming the diagnosis have been developed. The most recent vaccination guidelines and current treatment recommendations are discussed.

Historical note and terminology

Haemophilus influenzae was first isolated by Pfeiffer during the 1889 influenza pandemic (Pfeiffer 1893), and it was believed to be the causative agent of influenza. It was called the “influenza bacillus.” Eventually, the error of this diagnostic association was recognized. The organism was given the genus name Haemophilus, meaning “blood-loving,” and the species name influenzae in recognition of the historical association.

Clinical manifestations

Presentation and course

Meningitis is the most serious form of Haemophilus influenzae type b (Hib) disease. The history of an upper respiratory tract infection preceding onset of meningitis frequently can be obtained. Meningitis symptoms typically include fever, headache, nausea, vomiting, irritability, and lethargy proceeding to further clouding of consciousness and, ultimately, death. Clinical signs include evidence of meningeal irritation, though this can be lacking in neonates, the elderly, and the deeply comatose. Focal signs may also appear, probably reflecting a complicating vasculitis. The course is frequently fulminant, with rapid neurologic deterioration leading to respiratory arrest and death (Jacobs et al 1983). Therefore, initiation of appropriate antibiotic treatment must not be delayed. From an initial respiratory infection, the bacteria typically spreads to the meninges hematogenously; therefore, it is no surprise that vasogenic shock frequently occurs (Naqvi et al 1986). For similar reasons, Hib meningitis is frequently associated with other blood disorders including coagulopathy, purpura, and anemia (Shurin et al 1986).

Non-type b H influenzae can also cause meningitis and manifests similarly to Hib meningitis. One study, from Papua New Guinea, found that 15% of H influenzae meningitis cases are due to non-type b encapsulated strains (Gratten et al 1985a; Gratten et al 1985b). Several reports suggest that disease, including meningitis, due to non-type b encapsulated H influenzae is also increasing in the United States (Fountain et al 1995; Nitta et al 1995; Centers for Disease Control and Prevention 1998), and the mortality rate of 1 of these strains, type F, is as high as 20% in children and 30% in adults (Urwin et al 1996).

Unencapsulated, nontypeable strains of H influenzae can also cause meningitis. However, these strains usually spread by direct extension from a focus of infection, rather than hematogenously (Saint Geme 2003). Thus, most patients who
develop nontypeable *H influenzae* meningitis have a preceding nontypeable *H influenzae* sinusitis or otitis media. Patients can also develop nontypeable *H influenzae* meningitis after head trauma, after a neurosurgical procedure, or if they have another cause of a cerebrospinal fluid leak. In fact, because of the association with the presence of a CSF leak, nontypeable *H influenzae* is a relatively common cause of recurrent bacterial meningitis (van Driel et al 2008). Though the CSF leak can be difficult to diagnose and repair, the possibility should be carefully evaluated in any case of nontypeable *H influenzae* meningitis because repair can prevent recurrence (Sprekelsen et al 2005).

Due to its life-threatening nature, meningitis is usually the predominant clinical concern when it develops in patients with *H influenzae* infection. However, presence of meningitis does not exclude the presence of the other complications of this infection as well. As a respiratory pathogen, the most typical coexisting complications will be seen to affect the upper or lower airways. Epiglottitis is seen most often in children, involves edema of the upper airway, and can be life-threatening because acute airway obstruction can occur. It usually occurs prior to development of meningitis and may be the manifestation that brings the patient to the hospital. Symptoms are often sudden in onset and include high fever, pharyngitis, stridor, cough, and dyspnea. As the throat closes, the child is unable to swallow, secretions pool, and drooling occurs. Some of the warning symptoms may be lacking, and throat closure can be rapid. Rapid recognition of respiratory infection is important because death can occur within hours unless an airway is established (Saint Geme 2003).

Concomitant pneumonia is frequent in patients with Hib meningitis. Hib pneumonia typically has an insidious onset compared to many other bacterial pneumonias and may become clinically important either before or after onset of meningitis. On chest x-ray, the infiltrate usually appears lobar, and often there is an associated pleural effusion. Unfortunately, the infection can spread directly to the pericardium, causing a purulent pericarditis (Garg et al 2006). This complication may initially manifest as severely worsening dyspnea and tachycardia, but can eventually lead to cardiac failure. However, with proper monitoring and treatment, outcome in patients with Hib pneumonia can be good (Saint Geme 2003).

Other complications of *H influenzae* infection include pyogenic arthritis and osteomyelitis, especially in children under 2 years old and usually in a single large joint (Fink and Nelson 1986). Sometimes arthritis can develop after a week or more of treatment for *H influenzae* meningitis. These latter cases are frequently culture negative, generally considered a reactive inflammation, and attributed to immune complex deposition in the joint (Rush et al 1986).

There is no typical rash associated with *H influenzae* infection that can help in making the diagnosis, as there is for other bacterial meningitides. However, in young children who become bacteremic with *H influenzae*, a warm, tender cellulitis can develop, usually affecting the face. The facial location and violaceous color of this cellulitis can suggest the diagnosis (Saint Geme 2003). Because this cellulitis develops in the setting of bacteremia, patients with cellulitis are at increased risk for the bacteria to seed yet another location, such as the meninges. Meningitis develops in up to 10% of children with *H influenzae* cellulitis (Ginsburg 1981; Baker and Bausher 1986; Chartrand and Harrison 1986).

Other manifestations of *H influenzae* infection include otitis media, conjunctivitis, sinusitis, urinary tract infection, and peritonitis. There was a recent case report of septic thrombosis of the cavernous sinus due to *Haemophilus influenzae* (Pavlovich et al 2006). A strain of nontypeable *H influenzae* has been linked to a case of Fisher syndrome via molecular mimicry (Houlston et al 2007).

**Prognosis and complications**

Complications during acute illness are similar to those seen with meningitides of any etiology and include subdural effusion, empyema, ischemic or hemorrhagic stroke, cerebritis, ventriculitis, abscess, and hydrocephalus (Saint Geme 2003).

**Biological basis**

**Etiology and pathogenesis**

*Haemophilus influenzae* is a small (0.3 to 1.0 µm), gram-negative coccobacilli, sometimes appearing in short chains. They can grow under both aerobic and anaerobic conditions. They are nonmotile and often are difficult to visualize in clinical specimens.

Six distinct serotypes of *H influenzae* have been identified based on the structure and antigenicity of their
polysaccharide capsules. These are designated types A through F. A 2-step, real-time, PCR-based assay that can differentiate all 6 capsulation loci in clinical specimens with high sensitivity and specificity has recently been developed (Maaroufi et al 2007). Additionally, nonencapsulated serotypes are identified based on failure to react with antisera against capsules of type A through F, and these are termed “nontypeable.” A PCR-based assay for identifying nontypeable *Haemophilus* has also been developed recently (Billal et al 2007).

Typical, community-acquired *H influenzae* meningitis is usually caused by type b, whereas meningitis developing as a result of risk factors such as sinusitis or head trauma is usually caused by nontypeable *H influenzae* (Pittman 1931; Turk 1984).

Encapsulated *Haemophilus influenzae* is transmitted by the respiratory route. Many individuals, particularly school-aged children, are asymptptomatically colonized (Spinola et al 1986; Oh et al 2008). Development of symptomatic infection largely has been attributed to host factors. These include exposure to cigarette smoke, coinfection with a viral respiratory pathogen, and probable genetic susceptibilities related to local respiratory immune function and anatomy (Saint Geme 1993).

Various bacterial factors have also been identified that assist in pathogenicity. The bacteria have factors that promote adherence to respiratory mucous and epithelial cells (Weber et al 1991; Saint Geme and Cutter 1995; Rao et al 1999; Kubiet et al 2000). Interestingly, a recent study suggested that viral coinfection can increase expression of receptors for bacteria, including non-typeable *H influenzae*, thus, promoting bacterial adhesion to respiratory epithelial cells, colonization, and possibly subsequent disease (Avadhanula et al 2006). *H influenzae* also has several mechanisms to evade the respiratory tract's immune response, including production of IgA protease, antigenic variation, and microcolony formation (Kilian and Poulsen 1992; Duim et al 1996; Duim et al 1997; Hendrixson and Saint Geme 1998). Several components of the bacteria's capsule interfere with mucociliary clearance from the lung. These include the lipo-oligosaccharide lipid A, peptidoglycan, and a glycerophosphodiesterase called protein D (Johnson and Inzana 1986; Kanthakumar et al 1996; Janson et al 1999).

Transient bacteremia probably occurs relatively frequently and is related to the bacteria’s ability to adhere to and enter the epithelial cells and penetrate the epithelial tight junctions of the nasopharynx and respiratory tract (Saint Geme and Falkow 1990; Weiser et al 1990; Stephens and Farley 1991; van Schilfgaarde et al 1995; van Schilfgaarde et al 2000a; van Schilfgaarde et al 2000b). *H influenzae* type b (and probably other encapsulated types) is more likely than nontypeable *H influenzae* to persist in the blood and seed distant sites such as the meninges because the type b polysaccharide capsule promotes evasion of immune recognition and resistance to phagocytosis (Saint Geme 2003). In vitro and animal models, strains of *Haemophilus* associated with invasiveness and meningitis interact with toll-like receptors, particularly -2 and -4, to trigger an inflammatory response (Morgensen et al 2006) and a shift from Th1 to Th2 cytokines (Chen et al 2006).

**Epidemiology**

Prior to development of the Hib vaccine, Hib was found colonizing the nasopharynx of 3% to 5% of children and a smaller percentage of adults (Kuklinska and Kilian 1984). Hib was the leading cause of bacterial meningitis in children under 5 years of age and accounted for 8000 to 10,000 cases per year in the United States (Cochi and Broome 1986). Both colonization and meningitis due to this organism have now been nearly eradicated in infants and children (Bisgard et al 1998; Rosenstein and Perkins 2000), who are routinely vaccinated. Nontypeable strains, on the other hand, continue to colonize 40% to 80% of both children and adults (Kuklinska and Kilian 1984), frequently causing otitis media but rarely causing severe disease.

Prior to the vaccine, approximately 1 in 200 children in the United States developed bacteremia with this organism, along with its associated complications, including meningitis, by the age of 5 years. Peak incidence was 6 to 7 months of age (Saint Geme 2003). Again, these complications have largely been eradicated in vaccinated populations (Hufnagel et al 2008). With vaccination of children, the epidemiology of *Haemophilus influenzae* has shifted toward an adult age distribution and also toward woman, perhaps as unvaccinated primary caregivers for children (Farhoudi et al 2005).

Ethnic groups at risk include African Americans, Alaskan Eskimos (Ward et al 1981; Galil et al 1999), and Native Americans (Coulehan et al 1976; Santosham et al 1987). Even with good vaccine coverage, Native Alaskans have higher rates of *H influenzae* disease than non-Native Alaskans and other U.S. children, probably due to other
environmental and household factors contributing to transmission (Singleton et al 2006). Additionally, serotype replacement with non-type b strains has resulted in a re-emergence of invasive disease in these children (Bruce et al 2008). Other risk factors include childcare center attendance and overcrowded living conditions (Parke et al 1972; Granoff and Basden 1980). Of course, the greatest risk factor is inadequate vaccination. More than 20% of children in the United States in 2003 were undervaccinated for H influenzae type b for longer than 6 months within the first 24 months of life (Luman et al 2005). Factors associated with severe delay in childhood vaccination include being raised by a single parent, by an uneducated parent, in a multiple child household, and African American race.

It is also still important to consider the possibility of Hib-associated meningitis in patients who come from the developing world. Vaccines are unavailable to most people in many of these countries, and the etiologic shift in bacterial meningitides of the young, which has occurred in the United States, has not occurred in these countries. In fact, as of 2000, use of the vaccine had led to a worldwide decrease in incidence of Hib meningitis of only 5.7% (Peltola 2000). H influenzae still accounts for approximately 500,000 deaths per year in children under 5 years old, many of these due to meningitis (Levine et al 1998).

Another important population at risk includes those with medical conditions that produce immunocompromise, especially compromise of the ability to clear encapsulated organisms. Such conditions would include asplenia (anatomic or functional), sickle cell disease, HIV infection or IgG2 subclass deficiency, chemotherapy, and bone marrow transplantation (Saint Geme 2003). Unfortunately, the Hib vaccination may not be as effective in some of these conditions, such as in those with HIV infection (Madhi et al 2005). Vaccination of bone marrow donors prior to transplant may improve antibody concentrations in recipients after transplant (Parkkali et al 2007).

**Prevention**

There are currently at least 5 highly effective vaccines to prevent infection with Haemophilus influenzae type b. These vaccines conjugate the capsular antigen of type b, polyribose-ribitol phosphate, to an immunogenic adjuvant. The available vaccines essentially differ in the choice of adjuvant and type of linkage between adjuvant and capsular antigen. As a result, they have slightly differing immunogenicities, and it is important to read the prescribing information for each vaccine to make sure it is administered appropriately. For example, some of the vaccines require a series of 4 injections and some require 3 injections. All of the vaccines are well tolerated, highly effective, and can be administered at the same time as other vaccines (American Academy of Pediatrics 2009).

The Hib vaccine is one of the greatest recent success stories in the field of neurology and, indeed, all of medicine. Until the mid-1980s, Hib was the leading cause of bacterial meningitis in children under 5 years old and accounted for 8000 to 10,000 cases per year in the United States (Cochi and Broome 1986). Both colonization and meningitis due to this organism have now been nearly eradicated in infants and children (Bisgard et al 1998; Rosenstein and Perkins 2000) who are vaccinated.

There are no currently available vaccines that offer protection against non-type b H influenzae.

A bacterial polysaccharide immunoglobulin preparation is also available for passive immunization. It is prepared from the plasma of adult donors immunized with Hib, meningococcal, and pneumococcal polysaccharide vaccines. It is useful for immunocompromised patients who lack an active immune response to vaccine and for prevention of disease in certain other groups at highest risk for disease during infancy, including Native Americans and Eskimos. Protective levels of anti-type b capsular antibody persist in the serum for up to 4 months after injection with this immunoglobulin (Ambrosino et al 1986). A clinical trial demonstrated significant protection against severe Hib infection in Native American children given 3 doses during the first year of life (Santosham et al 1987).

When a case of Hib is discovered in a household with 1 or more children under 12 months of age, with children under 4 years who have not been adequately vaccinated, or with immunocompromised children, everyone in the household should receive prophylaxis with rifampin. This effectively prevents spread of disease and decreases incidence of severe disease, including meningitis. Similar guidelines are suggested for all children and personnel at a childcare center that has experienced 2 cases within a 60-day period. Prophylaxis after a single case at a childcare center is controversial (American Academy of Pediatrics 2009).

Prophylaxis with amoxicillin or sulfisoxazole may be useful in preventing spread of disease and incidence of severe disease in children who have recurrent otitis media from nontypeable H influenzae.
**Differential diagnosis**

The history and examination data obtained from any given case of acute bacterial meningitis can be variable. This is especially true for young children, the most common patient population to get *Haemophilus influenzae* meningitis. Invariably, some of the typical findings are present, whereas others are absent. Additionally, the signs and symptoms frequently seen with acute bacterial meningitis, including fever, behavioral or personality changes, and mental status changes, can be nonspecific and suggest other diagnoses, including systemic infection or sepsis, viral encephalitis or meningitis, fungal or tuberculous meningitis, trauma or closed head injury or child abuse, multiple metabolic abnormalities (hypoglycemia, ketoacidosis, electrolyte imbalance, uremia, toxic exposure), seizure, and brain tumor. Even meningismus, which is often not present in children, does not exclude alternative diagnoses such as subarachnoid hemorrhage, intracranial hemorrhage, and epidural abscess. In order to prevent morbidity and mortality from missed diagnoses, it is important to keep a low index of suspicion for acute bacterial meningitis and err on the side of starting treatment early and unnecessarily.

Prior to widespread use of the Hib vaccine, *H influenzae* type b was the leading cause of acute bacterial meningitis in children under the age of 5 years (Cochi and Broome 1986). It is still prevalent in developing countries but is largely eradicated in the United States (Bisgard et al 1998; Rosenstein and Perkins 2000). Now, *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common etiological agents in children after the neonatal period. In children under 1 year of age, group B streptococci and gram-negative enteric bacilli, particularly *Escherichia coli*, are the leading etiologic agents, presumably because of exposure to these agents during birth. Due to passive transfer of maternal antibodies, these neonates did not typically develop *H influenzae*, streptococcal meningitis, or meningococcal meningitis, even prior to the use of the vaccine.

In the setting of a preceding sinusitis, otitis media, head trauma, neurosurgical procedure, or cerebrospinal fluid leak, *S pneumoniae* and nontypeable *H influenzae* are both common etiologic agents of recurrent meningitis (van Driel et al 2008), as both are a common part of “normal” skin and nasopharyngeal colonization. A recent study provides good evidence that surgical repair of CSF leak of various origins effectively prevents recurrent bacterial meningitis (Sprekelsen et al 2005).

In patients over 50 years of age, the most common causes of bacterial meningitis include *S pneumoniae* and gram-negative bacilli (Gorse et al 1984; Rasmussen et al 1992). *H influenzae* is included in the gram-negative group, along with *E coli*, *Enterobacter*, and *Pseudomonas*. *S pneumoniae* is more likely in association with pneumonia, *Pseudomonas* in association with chronic lung disease, *E coli* or *Enterobacter* in the setting of chronic urinary tract infection, and *H influenzae* in the setting of sinusitis, otitis media, head trauma, or a neurosurgical procedure. *Listeria monocytogenes* can also be seen, especially in the immunosuppressed elderly, and *S aureus* in neurosurgical patients.

**Diagnostic workup**

Bacterial meningitis, including that caused by *H influenzae*, should be considered and promptly treated in any patient with a compatible presentation—keeping in mind that the presentation may be atypical in some patients, especially young children. CSF examination showing a predominantly neutrophilic pleocytosis is strongly suggestive of bacterial meningitis and should prompt broad coverage treatment; though, in the proper clinical setting, treatment should not even be delayed in order to obtain CSF. Brain imaging should also be considered prior to CSF examination because many of these organisms, including *H influenzae*, can cause enough brain edema to make a lumbar puncture hazardous. No tests currently available to confirm *H influenzae* as the causative organism are rapid enough to base initial treatment on. The main value of these tests, therefore, is to confirm the correct initial clinical diagnosis.

With *H influenzae* meningitis, both blood and CSF cultures will usually be positive. However, again, treatment should be initiated without delay, even prior to obtaining culture samples. Gram stain of the CSF will be positive for gram-negative coccobacilli in approximately 70% of cases (Saint Gme 2003). The capsular polysaccharide of Hib can also be detected from serum, CSF, and urine by multiple methods, including latex particle agglutination, immunoelectrophoresis, and enzyme immunoassay. These techniques are usually more rapid than culture and may be useful even in patients with sterile cultures (Saint Gme 2003). One must be aware that vaccination for Hib can produce false positive reactions on these capsular antigen detection assays for days to weeks after vaccination (Scheifele et al 1989; Sood et al 1990; Jones et al 1991; Darville et al 1992; Goepp et al 1992). A simultaneous single tube PCR assay for detection of *Neisseria meningitidis*, *Haemophilus influenzae* type b, and *Streptococcus pneumoniae*
has been developed, and it has 88% sensitivity and 100% specificity for \textit{H. influenzae} meningitis (Failace et al 2005; Tzanakaki et al 2005). A 2-step real-time PCR-based assay that can differentiate all 6 capsulation loci in clinical specimens with high sensitivity and specificity has recently been developed (Maaroufi et al 2007), as has a PCR-based assay for identifying nontypeable \textit{Haemophilus} (Billal et al 2007).

**Management**

When bacterial meningitis is suspected, emergent antibiotic treatment must be initiated, without waiting for speciation to be made. Due to widespread use of the \textit{H. influenzae} vaccine, \textit{H. influenzae} is no longer considered to be a common etiology for community-acquired meningitis, even in children (Cochi and Broome 1986; Bisgard et al 1998; Rosenstein and Perkins 2000). Treatment is, therefore, directed primarily against \textit{S. pneumoniae} and \textit{N. meningitidis}. Current recommendations (Auwaerter 2009) for treatment of community-acquired meningitis for ages 3 months to 50 years is vancomycin 15 mg/kg IV every 8-12 hours (up to 2 g/day, maintaining serum trough levels of 15-20 ug/mL) plus either cefotaxime 50 mg/kg IV every 4 to 6 hours (maximum 2 g IV every 4 hours) or ceftriaxone 50 to 100 mg/kg IV every 12 hours (maximum 2 g IV every 12 hours). For patients with a penicillin or cephalosporin allergy, the recommended treatment is chloramphenicol 1 g IV every 6 hours plus vancomycin.

After speciation of \textit{H. influenzae}, the cephalosporin, either cefotaxime or ceftriaxone, is continued. Both have potent activity against \textit{H. influenzae}, and both penetrate the CSF well (Auwaerter 2009; Goldwater 2005). Total duration of treatment is 10 to 14 days. Amoxicillin was historically the treatment of choice for specific \textit{H. influenzae} therapy. However, resistance to amoxicillin is now 40% or more, and amoxicillin is not typically used as monotherapy any longer (Doern et al 1997; Kaczmarek et al 2004; Saha et al 2005). The increase in resistance is due both to beta-lactamase producing strains and mutations in penicillin binding proteins. It is occurring around the world, suggesting and supporting the economic benefit of prevention through increased availability of immunization (Fluit et al 2005; Scott et al 2005; Hasegawa et al 2006).

For patients with cephalosporin allergy, chloramphenicol can be continued. Chloramphenicol is bactericidal for \textit{H. influenzae} and reliably penetrates the CSF (Anonymous 1999; Auwaerter 2009). However, resistance to chloramphenicol may also be rising (Saha et al 2005).

Dexamethasone 0.15 mg/kg every 6 hours given 15 to 20 minutes prior to antibiotics for the first 4 days of therapy may also be beneficial for initial treatment of community-acquired bacterial meningitis, though this recommendation is still controversial (de Gans and van de Beek 2002; van de Beek et al 2004). Dexamethasone may be more useful for \textit{H. influenzae} meningitis than for other forms of bacterial meningitis, and the efficacy of early dexamethasone therapy for bacterial meningitis in children from the pre-\textit{H. influenzae} vaccine era is actually better established than it is in the post-vaccine era. Dexamethasone 0.15 mg/kg every 6 hours, initiated prior to the first dose of antibiotic and continued for the first 4 days of treatment, decreases the risk of mortality, severe hearing loss, and neurologic sequelae in adults and children with community-acquired bacterial meningitis (Lebel et al 1988; Odio et al 1991; Syrogiannopoulos et al 1994; van de Beek et al 2007). Overall, these results suggest that dexamethasone be strongly considered in any patient with suspected community-acquired bacterial meningitis, especially in children at risk for \textit{H. influenzae} meningitis.

In addition to medication therapies, it is imperative that appropriate supportive care be instituted. Advancements in intensive care techniques offer significant benefit for patients with bacterial meningitis, including \textit{H. influenzae} meningitis.

**Outcomes**

The prognosis of \textit{H. influenzae} meningitis, as with most bacterial meningitis, relates directly to early diagnosis and initiation of appropriate antibiotic therapy. With appropriate therapy instituted early, mortality is 5% or less. Morbidity, however, is high, even with the best possible treatment, and significant, permanent neurologic sequelae are observed in 30% to 50% of patients (Sell et al 1972; Feigin et al 1976). Acute neurologic complications are also associated with later behavioral and developmental difficulties (Taylor et al 1998; Taylor et al 2000), hearing loss, and seizures (McIntyre et al 1993; D’Angio et al 1995). \textit{H. influenzae} meningitis was once the leading cause of acquired mental retardation in the United States, with about a third of patients going on to have mental retardation (Brosco et al 2006). Mental retardation due to Hib has now been almost completely eliminated due to the vaccine.
Special considerations

Pregnancy

*Haemophilus influenzae* is the causative agent of approximately 6% of cases of pregnancy associated pneumonia (Lim et al 2003). Pneumonia in pregnancy significantly increases the morbidity and mortality of both the woman and the fetus. Little is known about the neurologic complications of *H influenzae* infection in pregnancy, but they are presumably similar to the complications seen in non-pregnant hosts. Treatment is also similar; the cephalosporins are felt to be safe in pregnancy. Little is known about the possibility of vertical transmission of *H influenzae* from mother to fetus, but it does not seem to be a significant issue.

Vaccination of pregnant women against the polyribophosphate capsular antigen of *Haemophilus influenzae* type b at 34 to 36 weeks' gestation leads to a large boost in their antibody levels against this antigen. This boost is transferred to their newborn infants, such that newborn serum antipolyribophosphate capsular antigen level at birth is 100-fold greater than that of control newborn infants. Furthermore, this antibody persists at a protective level for 12 months, whereas control newborn infants lose significant antibody by 3 months (Amstey et al 1985).

*H influenzae* may cause ascending fetal infection and death, and may cause maternal sepsis by fetomaternal transmission (Horvath et al 2008).

Anesthesia

*Haemophilus influenzae* is a relatively frequent cause of postoperative pneumonia and a rare cause of postoperative respiratory distress (Tebbutt 1986; Campbell 1990; Sales et al 1992).

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**References especially recommended by the author or editor for general reading.
ICD and OMIM codes

ICD codes

ICD-9:
Hemophilus meningitis: 320.0

ICD-10:
Hemophilus meningitis: G00.0

Profile

Age range of presentation

01-23 months
02-05 years
06-12 years
13-18 years
19-44 years
45-64 years
65+ years

Sex preponderance

male>female, >1:1

Family history

family history may be obtained

Heredity

none

Population groups selectively affected

Eskimo
Native American Indian
African American

Occupation groups selectively affected

child care center personnel

Differential diagnosis list

encephalitis
systemic infection
sepsis
viral encephalitis
viral meningitis
fungal meningitis
tuberculous meningitis
trauma
closed head injury
child abuse
hypoglycemia
ketoacidosis
electrolyte imbalance
uremia
toxic exposure
seizure
brain tumor
subarachnoid hemorrhage
intracranial hemorrhage
epidural abscess
*Streptococcus pneumoniae*
*Neisseria meningitidis*
Group B streptococci
gram-negative enteric bacilli
*Escherichia coli*
*Enterobacter*
*Pseudomonas*
*Listeria monocytogenes*
*S. aureus*

**Associated disorders**

Cellulitis
Epiglottitis
Pneumonia

**Other topics to consider**

Gram-negative bacillary meningitis
Headache associated with meningitis, encephalitis, and brain abscess
Molecular diagnosis of central nervous system infections
Recurrent meningitis
Vaccines for neurologic disorders